Bone Marrow Biopsy for the Initial Staging of Patients With Lymphoma: Too Soon to Toss the Trephine

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Although the prospect is tempting, we do not believe there are sufficient grounds at this time to abandon bone marrow biopsy in patients with lymphoma. It still provides robust prognostic information, and in the majority of patients it remains an indispensable staging tool.

Recent studies showing excellent sensitivity of $^{18}$F-fluorodeoxyglucose (FDG) positron emission tomography (PET)-CT for detecting marrow involvement in patients with Hodgkin lymphoma (HL)[1-3] and diffuse large B-cell lymphoma (DLBCL)[4] have led some to claim that bone marrow biopsy (BMB) is obsolete. The argument is that the low number of patients “upstaged” by positive BMB no longer justifies the pain, anxiety, and risk of complications.

Although invasive, BMB is quite safe if performed by an experienced operator; the risks of major bleeding (1:4,000, and largely restricted to patients with myeloproliferative neoplasms) and death (1:50,000) are low.[5] Patient anxiety can be allayed with good communication to establish trust and rapport, while pain can be minimized using generous local anesthesia, the offer of sedation, and analgesia.[6] A single trephine (length ≥ 20mm with analysis of multiple levels and appropriate immunohistochemistry) obviates the need for bilateral biopsies and maximizes the diagnostic yield.[7]

In patients with HL, the sensitivity of PET-CT for detecting bone marrow involvement is high, exceeding that of BMB, but the characteristics of patients identified by each procedure do not overlap completely. In the series of 454 patients assessed by El-Galaly et al, the reported sensitivity of PET-CT was 95%, compared with 31% for BMB.[1] Furthermore, there was no difference in 2-year progression-free survival between BMB-positive patients and those with negative BMB but multifocal skeletal lesions, suggesting the prognostic value of the finding was similar regardless of the means of determination. Pooled analysis of studies addressing this question suggests that 1% of patients with negative PET-CT have positive BMB and would be missed by omission of the procedure.[1,3,8-14] Although rare, such a finding has high clinical impact—particularly if treatment algorithms for limited-stage disease incorporate radiotherapy; in patients with a high International Prognostic Score, which is directly impacted by bone marrow status; or in patients who receive escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) rather than ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine).

In DLBCL, a recent study from the United Kingdom found the sensitivity of PET-CT (94%) was greater than that of BMB (40%) for detecting marrow involvement; however, the clinical significance of this finding is called into question by the lack of impact on patient outcomes of bone marrow involvement detected by PET (but not biopsy), compared with marrow involvement documented by histology, which predicted for an inferior outcome.[4] It is worth remembering that marrow involvement (equating to stage IV) thus potentially increases the score on the International Prognostic Index, which was generated in an era when BMB was standard. Furthermore, BMB can detect discordant marrow involvement in low-grade lymphoma. It appears that these patients have a greater tendency toward indolent relapse,[15,16] and one study has suggested benefit from up-front transplantation in such patients.[17] Such a management strategy is dependent upon thorough staging, including BMB. Finally, marrow involvement was identified as an independent risk factor for central nervous system involvement in older series[18,19]; however, more recent studies in patients treated with rituximab-containing chemotherapy regimens suggest that this may no longer be true.[20,21] Nonetheless, it appears to be too early to dispense with BMB in the management of
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DLBCL.

In mantle cell lymphoma (MCL), nearly all patients are shown to have marrow or gastrointestinal infiltration if sufficiently sensitive techniques are used.[22,23] Therefore, outside of a clinical trial, if all patients are treated as being at an advanced stage, BMB may be omitted without consequence. However, the European MCL Network has demonstrated that bone-marrow molecular remission is an independent predictor of superior clinical outcome[24]; post-induction minimal residual disease status has been incorporated into future trial protocols as a risk stratification criterion for maintenance/consolidation (M. Dreyling, personal communication).

Finally, in the case of indolent lymphomas such as follicular lymphoma, BMB remains a mandatory component of staging, as (1) marrow involvement is a specific component of the FLIPI-2,[25] and (2) limited-stage disease is treated with radiotherapy, while advanced-stage disease is observed or treated with systemic therapy.

Thus, although the prospect is tempting, we do not believe there are sufficient grounds at this time to abandon BMB in patients with lymphoma. BMB still provides robust prognostic information, and in the majority of patients it remains an indispensable staging tool. Many of the published series of PET assessment of bone marrow status are from academic tertiary referral centers with high scan volumes and considerable reporting expertise; the generalizability of their findings remains uncertain. Nevertheless, such sensitive imaging modalities are likely to replace BMB in selected scenarios, such as HL, once clear and reproducible internationally accepted criteria for positivity are established and validated in community practice settings.

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References:


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